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EXAMINER	
ZARA, JANE J	

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1635	

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06/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,001	GILCHREST ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-83* is/are pending in the application.

4a) Of the above claim(s) *1-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-17-09,3-21-09,12-28-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence Compliance Notice*.

DETAILED ACTION

This Office action is in response to the communication filed 4-29-09.

Claims 1-83 are pending in the instant application.

Election/Restrictions

Claims 1-77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4-29-09.

Applicant's election without traverse of Group XIX, claims 78-83, in the reply filed on 4-29-09 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 81 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of the term "the oligonucleotide or thereof" in line 1 of claim 81 cannot be determined.

Appropriate clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 83 is rejected under 35 U.S.C. 102(b) as being anticipated by Norton et al (Nature Biotech., Vol. 14, pages 615-619, 1996).

Norton et al (Nature Biotech., Vol. 14, pages 615-619, 1996) (See Document C45, IDS filed 4-17-09) teach compositions comprising an oligonucleotide comprising between 1-20 increments of TTAGGG, including GTTAGGGTTAG, which oligonucleotide is optionally a PNA or comprises phosphorothiate internucleotide linkages (see esp. Table 1 on page 616 and third full paragraph on page 618).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 78-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hitoshi et al (US 2002/0027167) in view of Norton et al (Nature Biotech., Vol. 14, pages 615-619, 1996)) (See Document C45, IDS filed 4-17-09) and Page et al. (Exp'l. Cell Res., Vol. 252, pages 41-49, 1999)) (See Document C48, IDS filed 4-17-09).

The claims are drawn to compositions comprising an oligonucleotide comprising between 1-20 increments of TTAGGG, optionally comprising GTTAGGGTTAG, or comprising at least 50% identity with these motifs, wherein the first nucleotide linkages on the 3'-end are hydrolyzable by a 3'-5' nuclease, and which oligonucleotide further comprises non-hydrolyzable linkages, which are optionally phosphorothioate internucleotide linkages, or which oligonucleotide is optionally a PNA.

Hitoshi et al (US 2002/0027167) teach nucleic acids encoding the nuclease MRE11, recombinant MRE11, various biochemical assays monitoring its exonuclease activity, its involvement in repairing DNA and chromosomal end-breaks, checkpoint regulation, cell cycle regulation and proliferative diseases. Hitoshi teaches methods of screening for modulators of MRE11 activity using synthesized substrates in various in vitro assays (see esp. abstract, pages 1-5, 11-13, figures 27-33).

Hitoshi does not teach the synthetic substrate sequences and the modifications instantly claimed.

Page et al. (Exp'l. Cell Res., Vol. 252, pages 41-49, 1999) teach compositions comprising a choice of various oligonucleotides with at least one increment of an oligonucleotide with at least 50% sequence identity with TTAGGG, which oligonucleotides also comprise non-hydrolyzable phosphorothioate internucleotide linkages for stability from nuclease degradation, and which oligonucleotide sequences are known to populate the 3' termini overhang of chromosomes (*a.k.a.* telomere overhang), and which 3' terminal overhangs are associated with high telomerase activity in immortal cells, transformed cells, mitogenic stimulation and proliferative diseases (see entire document, esp. the text on p. 41, second full paragraph on p. 42, Tables 1, 2 and Figures 1, 2 on pages 42-43)) (See Document C48, IDS filed 4-17-09)

Norton et al (Nature Biotech., Vol. 14, pages 615-619, 1996)) (See Document C45, IDS filed 4-17-09) teach compositions comprising an oligonucleotide comprising between 1-20 increments of TTAGGG, including GTTAGGGTTAG, which oligonucleotide is optionally a PNA or comprises phosphorothiate internucleotide linkages (see esp. Table 1 on page 616 and third full paragraph on page 618).

It would have been obvious to one of skill in the art to design and use the oligonucleotides instantly claimed to measure MRE11 activity because MRE11 was well known in the art to have 3'-5' exonuclease activity and to be involved in repairing DNA strand breaks and to be involved in the regulation of telomerase activity and in cell cycle regulation, as taught previously by Hitoshi et al. Furthermore, the motifs instantly claimed were all well known motifs existing as 3' telomerase overhangs, as taught previously by Page and Norton and many others in the field. One would have been

motivated to design the oligonucleotides claimed, including the incorporation of stabilizing modifications in the internal internucleotide linkages, as substrates to measure MRE11 exonuclease activity because the modifications claimed and the substrates claimed were taught previously by Norton and Page, phosphorothioate internucleotide linkages were well known to be stable to nuclease degradation, and PNAs were well known to provide oligonucleotide stability.

One would have reasonably expected that placing these modifications onto the substrates instantly claimed (e.g. internal linkages to comprise phosphorothioate linkages) would provide for appropriate substrates with which to monitor the 3-5' exonuclease activity of MRE11, without fully degrading the substrates. This design therefore would be reasonably expected to be suitable for measuring the exonuclease activity of MRE11 in vitro, and to be suitable in an assay to search for modulators of MRE11 in order to study the role of MRE11 in various cellular and pathological processes, including chromosomal repair, cellular senescence, proliferative disorders, and disorders reflecting the imbalance of telomerase and MRE11 activities.

For these reasons, the instant invention would have been obvious to one of skill in the art at the time of filing.

Sequence Compliance Notice

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37

CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **Please provide an appropriate SEQ ID No. for the sequence recited in claim 81, and any other places as appropriate in the specification.**

Please see the accompanying Notice to Comply.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
6-10-09

/Jane Zara/

Primary Examiner, Art Unit 1635